

CLAIMS

1. A compound comprising a target cell-specific portion and a cytotoxic portion characterised in that:
 - (i) the target cell-specific portion comprises an humanised monoclonal antibody having specificity for polymorphic epithelial mucin (PEM), or an antigen binding fragment thereof; and
 - (ii) the cytotoxic portion has endonucleolytic activity.
2. A compound according to Claim 1 wherein the target cell-specific portion comprises an humanised HMFG-1 antibody or an antigen binding fragment thereof.
3. A compound according to Claim 2 wherein the target cell-specific portion is an humanised HMFG-1 antibody.
4. A compound according to Claim 1 or 2 wherein the target cell-specific portion comprises an antigen binding fragment of the humanised antibody selected from the group consisting of Fab-like molecules, such as Fab and $F(ab')_2$, Fv molecules, disulphide-linked Fv molecules, ScFv molecules and single domain antibodies (dAbs).
5. A compound according to Claim 4 wherein the target cell-specific portion comprises a Fab molecule.
6. A compound according to Claim 4 wherein the target cell-specific

portion comprises a F(ab')₂ molecule.

7. A compound according to Claim 1 wherein the target cell-specific portion comprises an amino acid sequence encoded by at least part of one or both of the nucleotide sequences of Figure 3(a) and (d).
8. A compound according to Claim 7 wherein the target cell-specific portion comprises an amino acid sequence encoded by the nucleotide sequence of Figure 3(a) and an amino acid sequence encoded by the nucleotide sequence of Figure 3(d).
9. A compound according to any one of Claims 1 to 8 wherein the cytotoxic portion has DNA endonucleolytic activity.
10. A compound according to Claim 9 wherein the cytotoxic portion is at least the catalytically active portion of a DNA endonuclease.
11. A compound according to Claim 10 wherein the endonuclease is a mammalian deoxyribonuclease I.
12. A compound according to Claim 11 wherein the endonuclease is a human deoxyribonuclease I.
13. A compound according to Claim 1 wherein the endonuclease is a restriction endonuclease.
14. A compound according to Claim 10 wherein the cytotoxic portion comprises the amino acid sequence shown in Figure 2(a) or (b).

15. A compound according to any one of Claims 1 to 14 wherein a nuclear localization signal is incorporated.
16. A compound according to Claim 15 wherein the nuclear localization signal comprises the sequence PKKKRKV.
17. A compound according to any one of Claims 1 to 16 wherein the target cell-specific portion and the cytotoxic portion are fused.
18. A compound according to Claim 17 wherein the target cell-specific portion and the cytotoxic portion are separated by a linker sequence.
19. A compound according to Claim 18 wherein the linker sequence is or comprises GG or GSGG.
20. A compound according to any one of Claims 1 to 19 wherein the compound comprises all or part of the amino acid sequence as shown in Figure 3(c) together with all or part of an amino acid sequence selected from the group consisting of amino acid sequences as shown in Figures 5(d), 6(d), 7(b), 8(b), 9(b), 10(b), 11(b), 12(b), 13(d), 14(d), 15(d), 16(c), 17(d), 18(d) and 19(d).
21. A compound according to Claim 20 wherein the compound comprises an amino acid sequence as shown in Figure 3(c) and an amino acid sequence as shown in Figure 7(b).
22. A compound according to Claim 20 wherein the compound comprises

an amino acid sequence as shown in Figure 3(c) and an amino acid sequence as shown in Figure 14(d).

23. A nucleic acid molecule encoding a compound as defined in any one of Claims 1 to 22.
24. A nucleic acid molecule according to Claim 23 wherein the molecule comprises all or part of the nucleotide sequence as shown in Figure 3(a or b) together with all or part of a nucleotide sequence selected from the group consisting of nucleotide sequences as shown in Figures 5(a, b and c), 6(a, b and c), 7(a), 8(a), 9(a), 10(a), 11(a), 12(a), 13(a, b and c), 14(a, b and c), 15(a, b and c), 16(a and b), 17(a, b and c), 18(a, b and c) and 19(a, b and c).
25. A nucleic acid molecule according to Claim 24 wherein the molecule comprises a nucleotide sequence as shown in Figure 3(b) and a nucleotide sequence as shown in Figure 7(a).
25. A nucleic acid molecule according to Claim 24 wherein the molecule comprises a nucleotide sequence as shown in Figure 3(b) and a nucleotide sequence as shown in Figure 14(c).
26. A nucleic acid molecule according to any one of Claims 23 to 25 wherein the molecule further comprises a Kozak consensus ribosome-binding site.
27. A vector comprising a nucleic acid molecule according to any one of Claims 23 to 26.

28. A host cell comprising a vector according to Claim 27.
29. A pharmaceutical composition comprising a compound according to any one of Claims 1 to 22 and a pharmaceutically acceptable carrier.
30. A compound according to any one of Claims 1 to 22 for use in medicine.
31. Use of a compound according to any one of Claims 1 to 22 in the preparation of a medicament for treating a mammal having said target cells to be destroyed.
32. A method of treating a mammal having target cells to be destroyed, the method comprising administering a compound according to any one of Claims 1 to 22 to said mammal.
33. A use according to Claim 31 or a method according to Claim 32 wherein the mammal is a human.
34. A use according to Claim 31 or a method according to Claim 32 wherein the target cells to be destroyed are cancer cells.
35. A use or a method according to Claim 34 wherein the cancer cells are epithelial cancer cells.
36. A use or a method according to Claim 35 wherein the cancer cells are ovarian, gastric, colorectal and/or pancreatic cancer cells.